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Photooxygenation of chiral dienol ethers: asymmetric synthesis of alkoxydioxines

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Abstract: The addition of $^1O_2$ to chiral dienol ethers provides a new route to alkoxydioxines (alkoxyendoperoxides). Depending upon substitution and geometry, the [4+2] cycloaddition is accompanied or even supplanted by [2+2] cycloaddition leading to alkene cleavage and/or ene-like reaction leading to allylic hydroperoxides. The diastereoselectivity of cycloaddition is ultimately limited by the conformational freedom of the dienol ether substrates.

Keywords: oxygen, singlet; peroxides; cycloadditions; dienes

As part of investigations of additions to chiral peroxycarbenium ions, we required a general route to enantiomerically enriched 3-alkoxy-1,2-dioxines (Fig. 1). Although we had previously reported two different asymmetric syntheses of alkoxydioxines based upon photocyclization of hydroperoxyenones,[1] neither was suitable for the current purpose. A route based upon an enzymatic dioxygenation was limited in the nature of the substrates acceptable to soybean lipoxygenase[2] while a more recent approach based upon radical rearrangement of 2-hydroperoxyalkenols is only suitable for asymmetric synthesis in the case of alkoxydioxines bearing alkyl substitution at C_3.[3] The [4+2] cycloaddition of singlet oxygen ($^1O_2$) to chiral 1,3-dienol ethers seemed to offer an efficient approach to the required alkoxydioxines.[4] While the cycloaddition of $^1O_2$ to dienol ethers has been previously reported,[5] we are unaware of any example involving the oxygenations of chiral acyclic dienol ethers. We now describe the first investigation of $^1O_2$ addition to chiral acyclic 1-alkoxy-1,3-dienes, including the effects of diene substitution, olefin geometry, and chiral auxiliary on the mode and stereoselectivity of the cycloadditions.

Our approach was based upon the oxygenation of dienol ethers derived from chiral alcohols (Figure 1). The chiral auxiliary would need to direct the approach of $^1O_2$, an small and reactive dienophile, towards one face of the dienol ether. We and others have demonstrated the ability of several classes of chiral auxiliaries to direct the approach of $^1O_2$ to tethered alkenes or dienes.[6-8]

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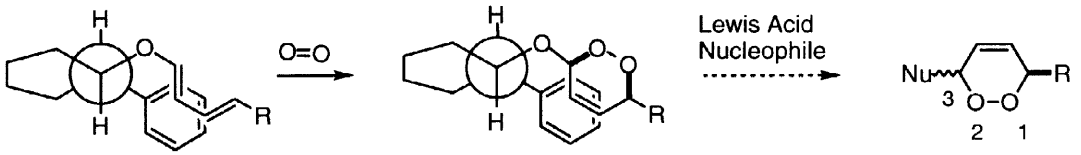


Figure 1: Auxiliary-Directed Oxygenation of Dienol Ethers

The diastereoselectivity of other Diels-Alder cycloadditions to chiral alkyl dienol ethers varies with the choice of chiral auxiliary (Figure 2). For example, the diastereoselectivity of cycloadditions with maleic anhydride increased on going from menthyl to phenethyl to arylcyclohexyl dienol ethers.[9] Stereoselection in cycloadditions with *N*-phenyl-1,2,4-triazoline-3,5-dione (PTAD), a dienophile generally considered similar in reactivity to $^1O_2$,[10] was poor for menthyl, moderate for phenmenthyl and phenylcyclohexyl-, and high for 2-mesitylcyclohexyl dienol ethers.[11]

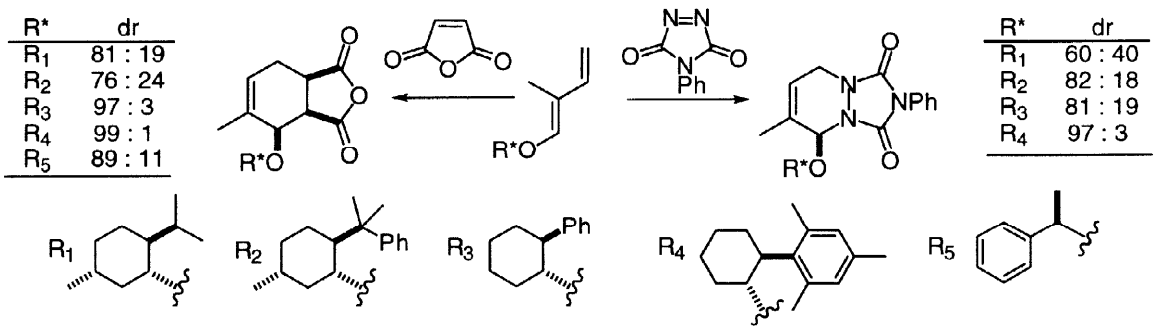


Figure 2: Diels-Alder Reactions of Chiral Dienol Ethers

Based upon these reports, we elected to compare the oxygenations of six classes of dienol ethers varying in substitution and diene geometry (Figure 3). The comparison of substrates with varying degrees of electron density and substitution would test the feasibility of cycloadditions on substrates capable of alternative reaction pathways, including ene reactions or [2+2] cycloadditions. The comparison of geometric isomers would examine the influence of diene conformer populations on reaction diastereoselectivity. Several different chiral auxilaries were investigated. Menthyl was chosen as an inexpensive and available substrate offering relatively limited facial shielding. The 2-phenylcyclohexyl auxiliary was anticipated to afford increased facial shielding, while the 1-phenethyl auxiliary was chosen to allow comparison with previously described Diels-Alder reactions.

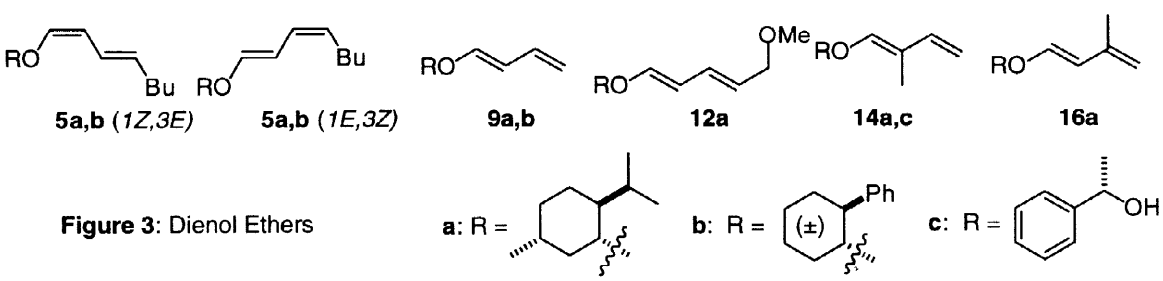
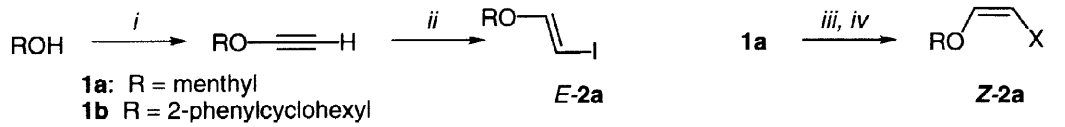


Figure 3: Dienol Ethers

RESULTS AND DISCUSSION

Dienol ethers were prepared by two general routes. Dienol ethers containing a Z-alkene in either the 1- or 3-position were prepared through semihydrogenation of enynol ethers.[12] Synthesis of substrates **5** began with alkynyl ethers **1a** and **1b** prepared from *L*-menthol and (*R,S*)-*trans*-2-phenylcyclohexanol by a reported procedure (Scheme 1).[13] Hydrozirconation and iodination led to 2-iodo enol ether *E*-**2a**;[14] the isomeric (*Z*)-**2a** was available through hydrostannylation/iodination.[15]



i. KH, THF, cat. imidazole, ROH, 0 °C; trichloroethene, -40 °C; *n*-BuLi, -78 °C; MeOH, -40 °C *ii.* ethynol ether, Cp_2ZrHCl, THF then I_2 *iii.* Et_3B, $HSnBu_3$; *iv.* THF, NIS

Scheme 1: Synthesis of Alkynyl and Haloenol ethers

Reaction of alkynol ethers **1** with a vinyl halide under Sonongashira conditions provided 3-en-1-ynol ethers **3**; the corresponding coupling of the iodoenol ether with an alkyne provided 1-en-3-ynol ethers **4**.[16,17] Selective semihydrogenation of the alkynes with P-2 Nickel or Lindlar's catalyst furnished the dienol ethers **5**. (Table 1).[18]

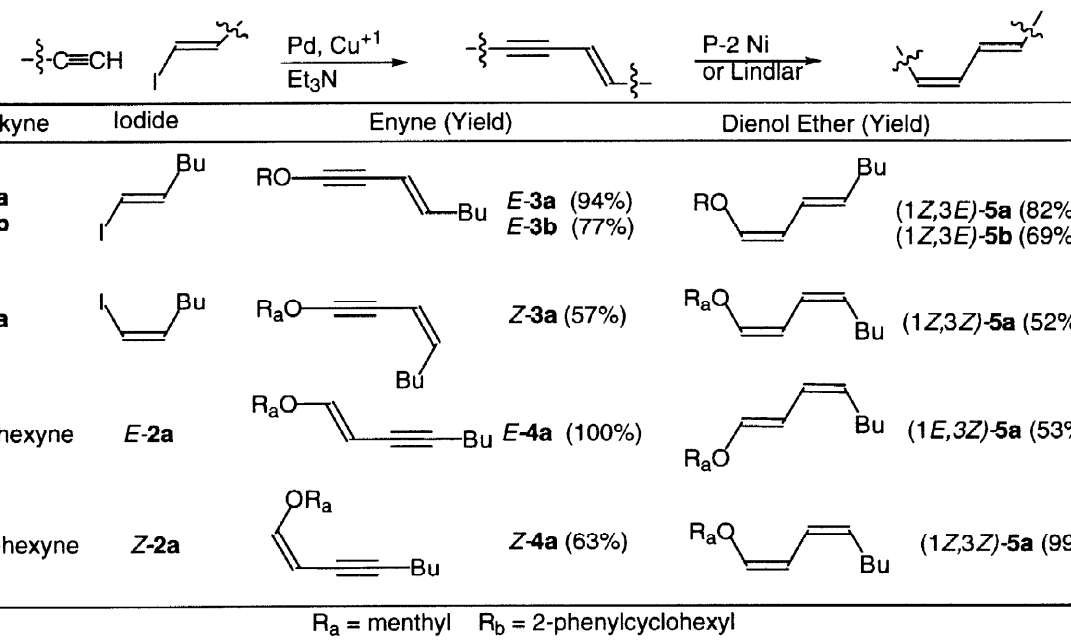
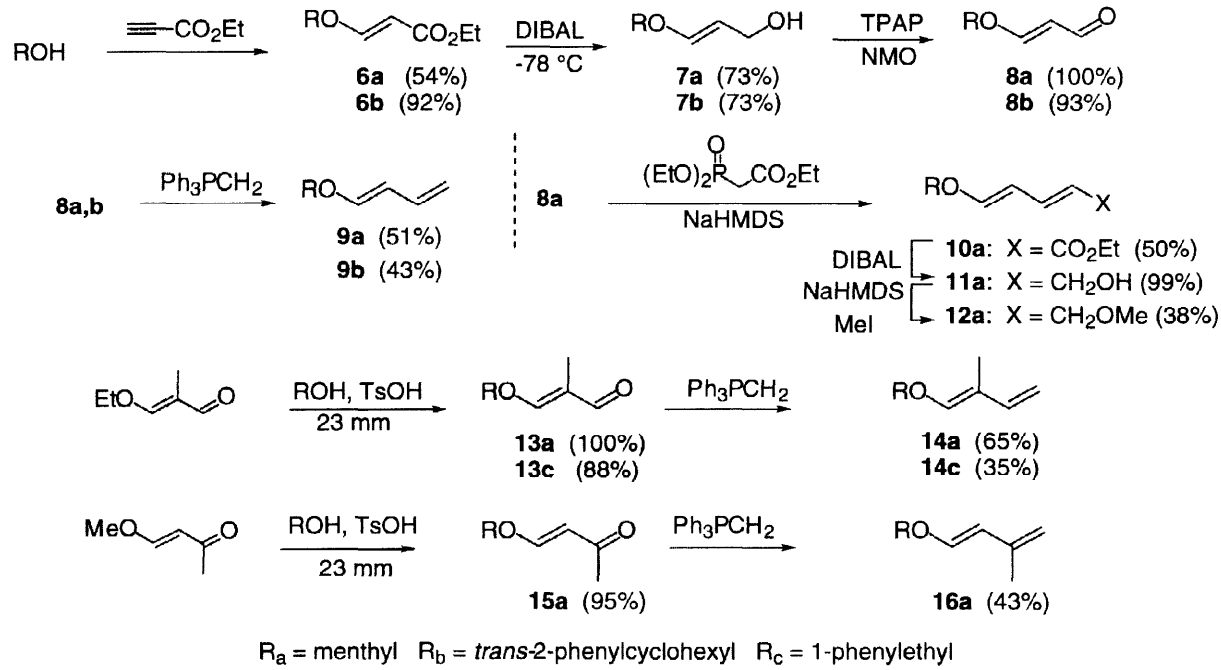


Table 1: Synthesis of Enynol and Dienol Ethers

Application of the aforementioned route to terminally unsubstituted dienol ethers was frustrated by overreduction. However, synthesis of dienol ethers **9ab** could be accomplished through Wittig methylenation of alkoxyenals **8ab** (Scheme 2).[19] Dienol ethers **14** and **16** were similarly prepared by methylenation of alkoxyenals (**13ac**) and an alkoxyenone (**15a**).[11,20] Although a functionalized E,E-dienol ether (**12a**) could be prepared based upon

Horner-Emmons olefination of **8a**, attempts to prepare simple 4-alkyl-E,E-dienol ethers via analogous Horner-Warren reactions were unsuccessful, as were attempts to perform hydride reductions of enynol ethers.



R_a = menthyl R_b = *trans*-2-phenylcyclohexyl R_c = 1-phenylethyl

Scheme 2: Wittig-based Synthesis of Dienol Ethers

Photooxygenations:

The dienol ethers were individually photooxygenated for 5 - 15 minutes at 0 °C in methylene chloride containing 0.02 m*M* tetraphenylporphyrin (TPP) using a 200 W visible lamp from a distance of 10-15 cm. Isolated yields and product ratios are shown in Table 2. With the exception of **20a** and **20c** (*vida infra*), the products were stable to the photooxygenation conditions. However, a number of the products underwent partial decomposition during purification. Consequently, product ratios were assessed by ^{1}H NMR following removal of CH_2Cl_2 *in vacuo* and redissolution of the crude products in $CDCl_3$.

The mode of reaction - Diels-Alder vs. ene vs. [2+2] - is sensitive to both substitution and geometry. Unsubstituted, 3-substituted, and 1Z,3E dienol ethers react exclusively via cycloaddition to afford excellent yields of alkoxydioxines. The sole E,E-dienol ether (**12a**) underwent oxygenation to form an endoperoxide (**19a**) as well as an alkoxyenal (**8a**) resulting from formation and cleavage of a dioxetane at the C3-4 alkene. The formation of dioxetanes during photooxygenation of dienol ethers has been previously observed.[21] The 1E,3Z- and 1Z,3Z- isomers of dienol ether **5a** underwent photooxygenation to furnish enal **8a**; no other products were observed in significant amounts. Although the crude NMR obtained following photooxygenation of 1Z,3Z-**5a** clearly showed the presence of both geometric isomers of **8a**, only the E-isomer was observed after purification, indicating the lability of the Z-enal towards isomerization. The regioselectivity of cleavage in formation of alkoxyenal **8** is analogous to that observed by Snider during oxygenation of a 1,4-dialkyl-1-methoxy-1,3-

dienyl ether and substantiates the FMO prediction of greater electron density at the remote alkene of simple alkadienol ethers.[1,22] The formate ester that would result from scission of the oxygen-bearing alkene was not observed.

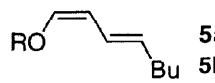
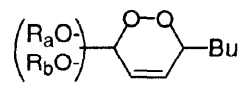
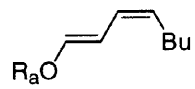
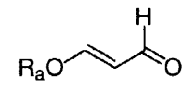
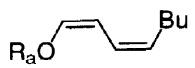
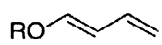
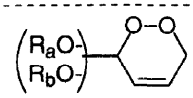
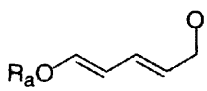
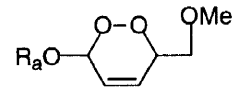
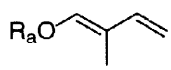
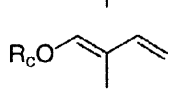
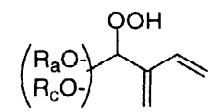
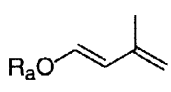
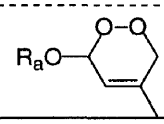
Dienol Ether		Product		Diast. Ratio		Yield
	**5a** *(1Z,3E)* **5b** *(1Z,3E)*		**17a** **17b**	62 : 38 74 : 26	(1.6 : 1) (2.9 : 1)	63 71
	**5a** *(1E,3Z)*		**8a**		NA	75
	**5a** *(1Z,3Z)*		**8a**		NA	99
	**9a** **9b**		**18a** **18b**	57 : 43 67 : 33	(1.3 : 1) (2 : 1)	86 79
	**12a**		**19a** **8a**	56 : 44	(1.25 : 1)	39 19
 	**14a** **14c**		**20a** **20c**	70 : 30 71 : 29	(2.3 : 1) (2.5 : 1)	na na
	**16a**		**21a**	53 : 47	(1.14 : 1)	90

Table 2: Oxygenations of Dienol Ethers

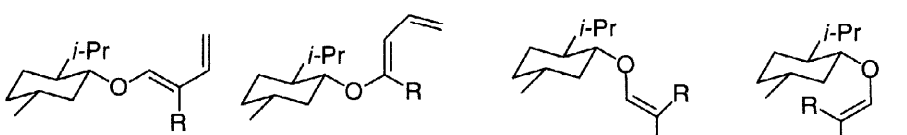
The 2-substituted dienol ethers **14a** and **14c** undergo ene-like reaction to furnish labile diene hydroperoxides **20a** and **20c**. The diastereoselectivity of these oxygenations was assessed at low (<50%) conversion; at high conversions, **20a** and **20c** began to undergo a second [4+2] addition of $^1O_2$ to form a hydroperoxide endoperoxide, a problem well precedented in the literature.[23,24] The selective formation of allylic hydroperoxides **20a** and **20c** from the 2-substituted dienol ethers **14a** and **14c** implies not only the selective formation of a perepoxide on the more substituted (and more hindered) internal alkene but also the preference of this perepoxide to undergo ene-like reaction via abstraction of an allylic hydrogen. In this context, it is surprising that the 3-substituted alkene **16a** undergoes cycloaddition rather than ene reaction.

Stereoselection:

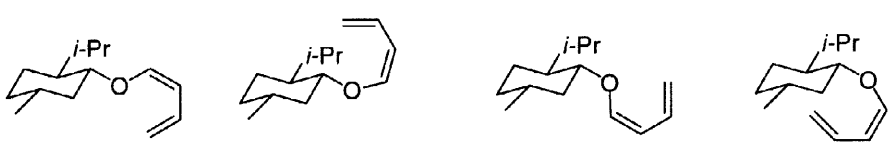
Reaction diastereoselectivity depends both on the conformational preferences of the dienol ether and on the ability of the chiral auxiliary to shield one face of the diene. The well-known

superiority of arylcyclohexyl compared with menthyl in shielding a neighboring trigonal center is to some degree reflected in our results.[23,25] However, the modest diastereoselection observed with the phenylcyclohexyl dienol ethers indicated a lack of conformational control, a hypothesis supported by the results of molecular modeling (Figure 4).[26] For brevity, conformational analysis is illustrated for terminally unsubstituted menthyl dienol ethers. With the exception of the 2-methyl dienol ethers, the diene unit of the dienol ethers was modeled while constrained to the *s-cis* dihedral necessary for Diels-Alder reaction. For the 1E dienol ethers the *syn* and *anti* conformers about the C-O-C=C dihedral were calculated to be within 0.4 kcal/mol. Previous results from our group and others have supported the assumption that $^1O_2$ is a reactive dienophile capable of giving a "snapshot" of the ground-state conformer population. Even assuming complete shielding of one face of a dienol ether by a chiral auxiliary, a difference of 0.4 kcal would predict maximum room temperature diastereoselectivity of 1.9 : 1 (66:34), a result similar to that observed for the phenycyclohexyl dienol ethers. In contrast, the lowest energy conformers of the 1Z-dienol ethers are separated by nearly 0.75 kcal/mol, predicting a diastereoselectivity of up to 3.5: 1. Diastereoselection approaching this level was in fact observed with the phenylcyclohexyl dienol ether **5b** (*1Z,3E*). For the 2-methylalkadienol ethers, two conformers presenting different prochiral faces, are calculated to be within 0.23 kcal/mol of one another. Because this substrate reacts via ene addition to the internal alkene, the conformer population was also modeled for the 2-methyl-1-propenyl (enol ether) analog; similar results were obtained. The observation of higher than expected reaction diastereoselectivity in this series may indicate the presence of other factors influencing this particular oxidation.

Figure 4: MM2 Steric Strain Energies (kcal/mol)

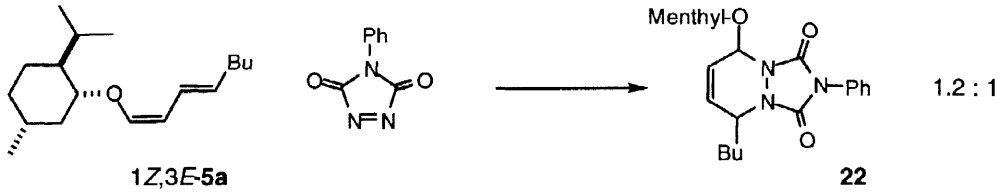


1E-dienol ethers (R = H)	16.8	17.2	18.5	22.3
2-Me dienol ethers (R = Me)	18.9	21.6	19.1	31.2



1Z-dienol ethers	20.46	>22.4	19.72	>28.1

PTAD reacts with alkenes through a similar mechanism as $^1O_2$.[27] Consistent with earlier reports, diene **5a** underwent rapid cycloaddition with PTAD to yield cycloadduct **22** as a 1.2 : 1 ratio of diastereomers.[11] Adam has recently observed PTAD to furnish superior diastereoselection relative to $^1O_2$ in a situation where stereochemical control was limited by dienophile approach. The failure to observe improved diastereoselection with PTAD supports the lack of conformational control as the primary contributor for limited diastereoselection.

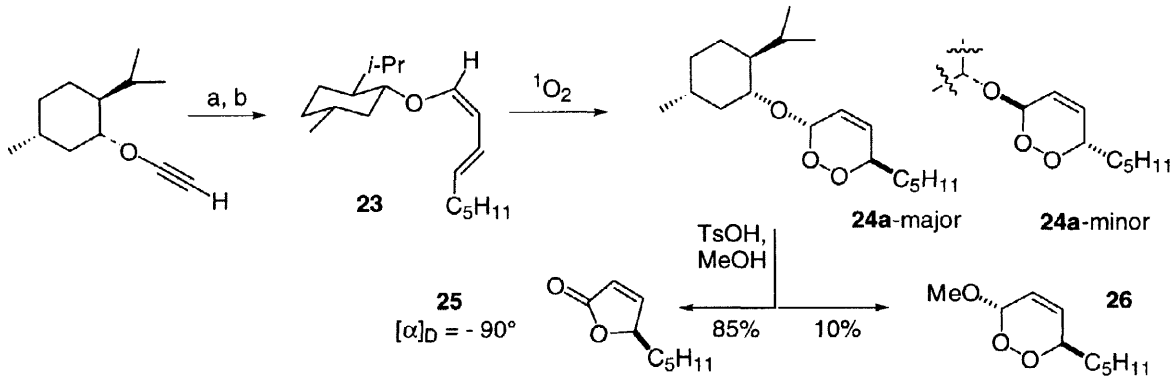


Scheme 3: Cycloaddition with PTAD

Assignment of Absolute Stereochemistry:

The absolute stereochemistry of an endoperoxide was assigned as illustrated in Scheme 4. Dienol ether **23** was prepared by an identical route as described earlier. Oxygenation furnished a 1.6 : 1 mixture of diastereomeric endoperoxides **24a**. Transetherification with acidic methanol was anticipated to provide 3-methoxyl-6-pentyl 1,2-dioxine, which had been previously been prepared in enantiomerically enriched form through a chemoenzymatic route. However, the hindered menthoxydioxine was surprisingly unreactive. Application of forcing conditions to the major alkoxydioxine diastereomer resulted in the predominant formation of (*R*)-butenolide **25**; the stereochemistry was assigned by the sign of rotation.[28,29] The butenolide was accompanied by small amounts of the (3*R*,6*R*)-methoxydioxine (**26**), identified through by comparison with a literature report for the (3*S*,6*S*) enantiomer.[2] The configuration of the products correlates with reaction of the Z,E-dienol ether **23** to form the (3*R*,6*R*) alkoxydioxine as the major isomer of **24a.**

Scheme 4: Stereochemical Correlation



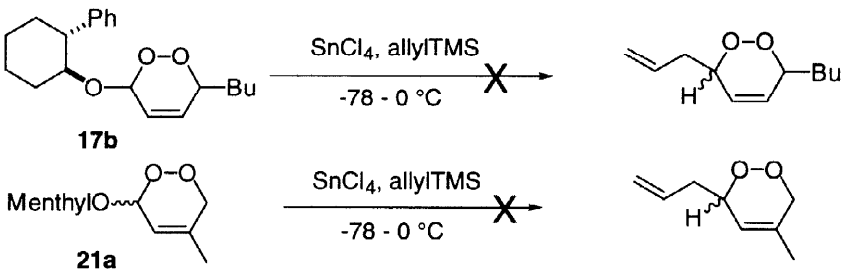
a. (*E*)-1-iodoheptene, $Pd(Ph_3P)_4$, CuI, *i*-$PrNH_2$; b. P2 Ni, H_2

Assuming approach of $^1O_2$ away from the isopropyl of the menthyl auxiliary, the favored formation of **24a** as the 3R,6R isomer is most easily rationalized as resulting from reaction of the dienol ether through a conformer with a *syn* C-O-C=C dihedral. Although this would seem to contradict the molecular modeling described above, recent experimental and theoretical work has indicated that cycloadditions of chiral enol ethers may proceed through transition states with reversed conformational preferences relative to ground states.

Application to Peroxycarbenium Chemistry:

We have previously described the displacement of peroxyacetals and peroxyketals, including 3-methoxy-1,2-dioxines, in the presence of Lewis acids (Scheme 5).[30] However, the resistance of the alkoxyendoperoxide towards transetherification (above) raised concerns

about the ease of peroxycarbenium ion formation and these concerns were borne out by the failure of **17b** and **21a** to undergo displacement under all conditions attempted.



Scheme 5: Attempted Lewis acid-mediated displacement

In conclusion, (1*Z*, 3*E*)-dienol ethers undergo 4+2 cycloaddition with the highest diastereoselectivity; (1*E*, 3*Z*)- and (1*Z*, 3*Z*)-dienol ethers undergo 2+2 cycloaddition at the (3*Z*)-alkene. The sole available example of a 4-alkyl substituted (1*E*, 3*E*)-dienol ether undergoes 4+2 cycloaddition with $^1O_2$ with only modest selectivity; Additionally, 2-alkyl substitution yields allylic hydroperoxides via ene reaction and 3-alkyl substitution affords peroxyacetals via 4+2 cycloaddition with essentially no stereoselectivity. The alkoxyendoperoxide products are ineffective as substrates for generation of the corresponding peroxycarbenium ions.

ACKNOWLEDGMENT

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EXPERIMENTAL

All reagents and solvents were used as supplied commercially, except THF and CH_2Cl_2, which were distilled from Na/Ph_2CO and CaH_2, respectively. NMR spectra were recorded in $CDCl_3$ unless otherwise noted; ^1H spectra are reported as (multiplicity, number of hydrogens, coupling constant in Hz). Infrared spectra were recorded as neat films unless otherwise stated. Selected absorbances are reported in wavenumber (cm^{-1}). Elemental analyses were obtained from M-H-W Laboratories (Phoenix, AZ), Desert Analytics (Tucson, AZ), or Quantitative Technologies, Inc., (Whitehouse, NJ). Progress of reactions involving peroxides were monitored by TLC, using an N,N'-dimethyl-*p*-phenylenediamine indicator hydroperoxides yield an immediate reddish-pink spot while peroxides exhibit a pink or green-red color after mild charring.[31] Chromatography was often performed with ethyl acetate/hexane which was recycled and quantitated by a reported procedure.[32] *Caution:* As in any work involving peroxides, standard precautions (use of protective equipment, minimal scale, avoidance of heat, light, or transition metal salts) should always be observed.[33-35]

Ethynyl, [2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether (1a)[13] and **ethynyl, [*trans*-2-phenylcyclohexyl (*R,S*)] ether (1b)** [36] were prepared according to literature procedures.

(*E*)-2-Iodoethenyl, [2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether (*E*-2a). To a flame dried flask under nitrogen and protected form light was added Cp_2ZrCl_2 (4.96 g, 17.0 mmol), THF (68 mL), and Super Hydride™ ($LiEt_3BH$, 16.0 mL, 1.0 M in THF). The mixture was stirred for 1 h whereupon ethynyl ether **1a** (1.53 g, 8.49 mmol) was added. After 15 min, iodine (2.37 g, 9.34 mmol) was added and the reaction stirred

for 10 min while protected from light. The reaction was diluted with ethyl acetate/hexane (EA/hex, ~50 mL). The organic layer was washed with sat. aq. $NaHCO_3$ (2 x 30 mL) and the combined aqueous layers were extracted with EA/hex. The combined organic layers were washed with 10% aq. Na_2SO_3 and sat. aq. NaCl, dried over sodium sulfate, concentrated, and purified by flash chromatography (100% pentane, Et_3N pretreated silica) to afford a clear, colorless oil (1.17 g, 45%): R_f 0.45 (100% hexane); $[\alpha]_D = -27°$ (c = 0.3, $CDCl_3$); ^1H NMR (360 MHz) 0.75 (d, 3H, *J* = 7), 1.33 (d, 3H, *J* = 2), 1.36 (d, 3H, *J* = 2), 1.37-1.41 (m, 5H), 1.25-1.41 (m, 2H), 1.62-1.67 (m, 1H), 2.05 (m, 1H), 3.56 (dt, 1H, *J* = 4, 11), 5.10 (d, 1H, *J* = 12), 6.68 (d, 1H, *J* = 12); ^{13}C NMR (75 MHz) 153.8, 81.1, 49.4, 47.6, 41.0, 34.2, 31.5, 25.8, 23.4, 22.0, 20.6, 16.3; FT-IR 2956, 2925, 2871, 1614, 1595, 1452, 1190, 1132 cm^{-1}; HRMS calcd for $C_{12}H_{21}OI$ (M^+) 308.0637, found 308.0634.

(*Z*)-2-Iodo-ethenyl, [2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether (*Z*-2a). To a stirred room temperature solution of **1a** (1.00 g, 5.50 mmol) and triethyl borane (0.55 mL, 1.0 M in hexane) under nitrogen was added tri-*n*-butyltin hydride (1.79 mL, 6.69 mmol). After 15 min at room temperature, a solution of *N*-iodosuccinimide (1.24 g, 5.50 mmol) in THF (25 mL) was added dropwise. The resulting solution was stirred at room temperature for 2 hours prior to concentration. The residue was subjected to column chromatography (100% pentane, Et_3N pretreated silica) to afford **2a** (1.34 g, 79%) as a clear, light yellow oil which decomposed upon storage: R_f 0.34 (100% hexane); $[\alpha]_D$ = -37° (c = 0.2 $CDCl_3$); ^1H NMR (300 MHz) 0.77 (d, 3H, *J* = 7), 0.89 (d, 3H, *J* = 3), 0.91 (d, 3H, *J* = 3), 0.94-1.48 (m, 5H), 1.61-1.70 (m, 2H), 1.93-2.00 (m, 1H), 2.13 (dsep, 1H, *J* = 3, 7), 3.61 (dt, 1H, *J* = 4, 11), 4.83 (d, 1H, *J* = 4), 6.64 (d, 1H, *J* = 4); ^{13}C NMR (75 MHz) 17.1, 21.4, 22.7, 24.2, 26.6, 32.3, 34.8, 42.2, 48.2, 51.3, 83.6, 152.2; FT-IR 2956, 2925, 2871, 1626, 1612, 1244, 1219, 1088, 1074, 987 cm^{-1}.

3*E*-Octen-1-ynyl, [2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)], ether (*E*-3a). To a solution of tetrakis(triphenylphosphine) palladium (500 mg, 0.558 mmol) in isopropyl amine was added (*E*)-1-iodo-1-hexene[37] (1.80 g, 8.56 mmol), **1a** (2.01 g, 11.15 mmol), and a solution of copper (I) iodide (163 mg, 1.12 mmol) in isopropylamine (5 mL). The resulting orange solution was stirred in the dark for 6 h. The reaction was diluted with hexane and thoroughly washed with ammonium chloride (sat. aq.). The aqueous layers were combined and extracted with hexane. The combined organic layers were dried over sodium sulfate, concentrated, and purified by flash chromatography (100% hexane, Et_3N pretreated silica) to afford a clear, light yellow oil (2.12 g, 94%): R_f 0.62 (100% hexane); $[\alpha]_D = -33°$ (c = 0.5, $CDCl_3$); ^1H NMR (300 MHz) 0.81 (d, 3H, *J* = 7), 0.84-1.54 (m, 18H), 1.60-1.70 (m, 2H), 2.00-2.08 (m, 2H), 2.12 (apparent dp, 1H, *J* = 3, 7), 2.22-2.29 (m, 1H), 3.80 (dt, 1H, *J* = 5, 11), 5.42 (dt, 1H, *J* = 15.5, 2), 5.89 (dt, 1H, *J* = 16, 7); ^{13}C NMR (75 MHz) 14.5, 17.0, 21.2, 22.6, 22.8, 24.1, 26.6, 31.9, 32.3, 33.3, 34.7, 39.8, 40.4, 47.6, 88.9, 96.9, 110.0, 141.3; FT-IR 3023, 2948, 2921, 2869, 2235, 1727, 1465, 1455, 1371, 1290, 1253, 948, 906, 756 cm^{-1}; Anal. Calcd. for $C_{18}H_{30}O$: C, 82.36; H, 11.54. Found: C, 82.25; H, 11.38.

3*E*-Octen-1-yne, [*trans*-2-phenylcyclohexyl (*RS*)] ether (*E*-3b) was prepared from **1b** (449 mg, 2.24 mmol) by a similar procedure in 77% yield (375 mg) after flash chromatography (100% hexane): R_f 0.66 (5% EA/hex); ^1H NMR (500 MHz) δ 0.95 (t, 3H, *J*= 9), 1.33-1.51 (m, 6H), 1.58 (dq, 1H, *J*= 3, 13), 1.68 (dq, 1H, *J*= 4, 12.5), 1.79-1.82 (m, 1H), 1.97-2.00 (m, 2H), 2.10 (dq, 2H, *J*= 1, 7), 2.46-2.49 (m, 1H), 2.81 (app dt, 1H, *J*= 4, 11), 4.15 (dt, 1H, *J*= 4.5, 11), 5.44 (dt, 1H, *J*= 1.5, 15.5), 5.92 (dt, 1H, *J*= 7, 15.5, 1H), 7.35-7.38 (m, 2H,), 7.26-7.31 (m, 3H); ^{13}C NMR (125 MHz) δ 13.8, 22.0, 24.6, 25.5, 31.0, 31.1, 32.5, 33.8, 39.8, 49.0, 89.4, 95.6, 109.3, 126.5, 127.5, 128.3, 140.6, 142.5; FT-IR 698, 754, 940, 995, 1253, 1449, 2245, 2858, 2930, 3028 cm^{-1}; HRMS calcd for $C_{20}H_{26}O$ (M^+) 282.1984, found 282.1973.

3*Z*-Octen-1-ynyl, [2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether] (*Z*-3a) was prepared in 57% yield from **1a** (300 mg, 1.66 mmol) and (*Z*)-1-iodo-1-hexene[38] (350 mg, 1.66 mmol) by a similar procedure as described above, except that pentane was employed for chromatography: R_f 0.58 (100% hexane); ^1H NMR (500 MHz) δ 0.79-1.05 (m, 8H), 0.83 (d, 3H, *J*= 7), 0.95 (d, 3H, *J*= 7), 1.22 (dt, 1H, *J*= 12, 12), 1.30-1.51 (m, 9H), 1.64-1.71 (m, 2H), 2.16 (app. dp, 1H, *J*= 3, 7), 2.20-2.28 (m, 3H), 3.84 (dt, 1H, *J*= 4, 11), 5.41 (dt, 1H, *J*= 10, 1.5), 5.68 (dt, 1H, *J*= 10, 7); ^{13}C NMR (125 MHz) δ 13.9, 16.3, 20.5, 22.0, 22.4, 23.4, 25.9,

29.6, 31.2, 31.6, 34.0, 37.8, 39.7, 46.8, 88.2, 101.3, 109.0, 139.6; FT-IR 903, 943, 1271, 1456, 2242, 2871, 2926, 2956, 3019 cm^{-1}; HRMS calcd for $C_{18}H_{31}O$: 263.2360, found 263.2375 $(M+H)^+$.

1*E*-Octen-3-ynyl, [2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether (*E*-**4a**) was prepared in quant. yield (455 mg) from (*E*)- **2a** (536 mg, 1.74 mmol) and 1-hexyne (0.19 mL, 1.7 mmol) using a similar procedure as described for **3a**: R_f 0.55 (100% hexane); $[\alpha]_D = -56°$ (c = 0.3, Et_2O); ^1H NMR (300 MHz) δ 0.74 (d, 3H, *J*= 7), 0.79-1.00 (m, 12H), 1.21-1.66 (m, 8H), 1.99-2.07 (m, 2H), 2.27 (dt, 2H, *J*= 2, 7), 3.49 (dt, 1H, *J*= 4, 11), 4.93 (dt, 1H, *J*= 2, 12.5,), 6.65 (d, 1H, *J*= 13); ^{13}C NMR (75 MHz) δ 13.6, 16.3, 19.2, 20.6, 21.97, 22.01, 23.4, 25.8, 31.1, 31.4, 34.2, 41.1, 47.5, 76.3, 81.7, 86.6, 88.3, 156.1; FT-IR 802, 1014, 1097, 1137, 1198, 1457, 1637, 2871, 2926, 2956 cm^{-1}; HRMS calcd for $C_{18}H_{30}O$ (M^+) 262.2289, found 262.2297.

1*Z*-Octen-3-yne, [2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether (*Z*-**4a**) was prepared from (Z)-**2a** (1.34 g, 4.33 mmol) and 1-hexyne (0.33 mL, 5.6 mmol) using a similar procedure as described above. Purification by flash chromatography (100% hexane, Et_3N pretreated silica) afforded **4a** (716 mg, 63%) as a clear, light yellow oil: R_f 0.60 (5% EA/hex); $[\alpha]_D = -35°$ (c = 0.2, $CDCl_3$); ^1H NMR (360 MHz) 0.78 (d, 3H, *J* = 7), 0.84-1.51 (m, 18H), 1.63-1.67 (m, 2H), 1.97-2.07 (m, 1H), 2.15 (apparent dp, 1H, *J* = 2.5, 7), 2.32 (dt, 2H, *J* = 2, 6), 3.52 (dt, 1H, *J* = 4, 11), 4.41 (d, 1H, *J* = 7, 2), 6.29 (d, 1H, *J* = 6); ^{13}C NMR (75 MHz) 153.4, 93.0, 85.0, 82.9, 75.1, 47.5, 41.4, 34.2, 31.6, 31.0, 25.9, 23.6, 22.1, 21.9, 20.6, 19.5, 16.5, 13.6; FT-IR 2954, 2927, 2870, 1631, 1456, 1369, 1344, 1257, 1163, 1093, 1074 cm^{-1}; Anal. Calcd. for $C_{18}H_{30}O$: C, 82.36; H, 11.54. Found: C, 82.53; H, 11.39.

1*Z*,3*E*-Octadiene, [2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether (1*Z*,3*E*-**5a**). Into an oven dried 3N flask, attached via a 3-way valve to an N_2 line and an H_2 balloon, was added $Ni(OAc)_2$ (45 mg, 0.18 mmol) and 5 mL of absolute ethanol. Following 3 cycles of vacuum and repressurization (nitrogen), the flask was charged with hydrogen. A solution of sodium borohydride (6.9 mg, 0.18 mmol) in 3 mL of absolute ethanol was added. After stirring for 20 minutes, ethylenediamine (0.045 mL, 0.72 mmol) and a solution of the enynol ether *E*-**3a** (50 mg, 0.19 mmol) in ethanol (2 mL) were added. After stirring for 1 h, hydrogen was purged and the reaction mixture was diluted with hexane. Following a wash with 10% aq. $NaHCO_3$, the organic layer was dried over Na_2SO_4. Concentration, followed by flash chromatography (100% pentane, Et_3N pretreated silica) afforded a clear, colorless oil (41 mg, 82%) containing an 82:18 mixture of the desired dienol ether and the over reduced enol ether. The two were separated using HPLC (0.05% EA/hex) to afford the pure enol ether **5a**: R_f 0.62 (100% hexane); $[\alpha]_D = -8°$ (c = 0.4, $CDCl_3$); ^1H NMR (300 MHz) 0.76 (d, 3H, *J* = 7), 0.85-1.41 (m, 18H), 1.60-1.68 (m, 2H), 1.92-2.18 (m, 4H), 3.39 (dt, 1H, *J* = 4, 11), 4.97 (dd, 1H, *J* = 11, 6), 5.50 (dt, 1H, *J* = 15, 7), 5.90 (d, 1H, *J* = 6), 6.34 (dd, 1H, *J* = 11, 15); ^{13}C NMR (75 MHz) 141.6, 131.1, 123.9, 106.9, 82.9, 48.4, 42.3, 35.0, 33.3, 32.5, 32.3, 26.5, 24.2, 23.0, 22.8, 21.4, 17.1, 14.6; FT-IR 2956, 2922, 2871, 1657, 1616, 1456, 1250, 1111, 1053, 970 cm^{-1}; HRMS calcd for $C_{18}H_{32}O$ (M^+) 264.2453, found 264.2451.

1*Z*,3*E*-Octadienyl, [*trans*-2-phenylcyclohexyl (*RS*)] ether (*1Z,3E*- **5b**) was prepared from ***E*-3b** (570 mg, 2.02 mmol) in 69% yield (396 mg) by a similar procedure: R_f 0.87 (5% EA/hex); ^1H NMR (360 MHz) δ 0.87 (t, 3H, *J*= 7, 3H), 1.60-1.24 (m, 8H), 1.74-1.79 (m, 1H), 1.85-2.01 (m, 3H), 2.13-2.19 (m, 1H), 2.66 (app dt, 1H, *J*= 4, 11), 3.63 (dt, 1H, *J*= 4, 10), 4.77 (dd, 1H, *J*= 6, 11), 5.37 (dt, 1H, *J*= 7, 15.5), 5.62 (d, 1H, *J*= 6), 6.08 (dd, 1H, *J*= 11, 15.5), 7.15-7.33 (m, 5H); ^{13}C NMR (75 MHz) δ 13.9, 22.2, 24.9, 25.8, 31.7, 32.5, 32.8, 33.4, 50.4, 84.5, 106.6, 123.1, 126.2, 127.7, 128.1, 130.2, 143.4, 143.6; FT-IR 698, 754, 970, 1075, 1108, 1448, 1615, 1656, 2856, 2927, 3029 cm^{-1}; HRMS calcd for $C_{20}H_{28}O$ (M^+) 284.2140, found 284.2142.

1*Z*,3*Z*-Octadienyl, [2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether (1*Z*,3*Z*- **5a**) was prepared from *Z*-**3a** (160 mg, 0.610 mmol) by the above procedure in 52% yield (83 mg, following HPLC purification (100% pentane), or from *Z*-**4a** (70 mg, 0.267 mmol) in 99% yield (70 mg) without purification: R_f 0.33 (100% hexane); $[\alpha]_D = -9°$ (c = 0.2, $CHCl_3$); ^1H NMR (500 MHz) δ 0.72-1.05 (m, 12H), 0.76 (d, 3H, *J*= 7), 1.25-1.42 (m, 6H), 1.62-1.66 (m, 2H), 1.97-2.02 (m, 1H), 2.05-2.15 (m, 3H), 3.42 (dt, 1H, *J*= 4, 10.5), 5.21 (dd, 1H, *J*= 6, 11), 5.25 (dt, 1H, *J*= 8, 11), 6.05 (d, 1H, *J*= 6), 6.33 (app t, 1H, *J*= 11); ^{13}C NMR (125 MHz) δ 13.9, 16.4, 20.7, 22.1, 22.4, 23.6, 25.9, 27.3, 31.6, 31.9, 34.3, 41.7, 47.8, 82.4, 101.9, 121.3,

128.2, 145.4; FT-IR 1049, 1103, 1245, 1263, 1602, 1647, 2871, 2921, 2955 cm^{-1}; HRMS calcd for $C_{18}H_{32}O$ (M^+) 264.2453, found 264.2443.

1*E*,3*Z*-Octadiene, [2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether (1*E*,3*Z*- **5a**) was prepared from *E*-**4a** (46 mg, 0.18 mmol) in 53% yield by the same procedure used for 1*Z*,3*E* **5a**: R_f 0.33 (100% hexane); $[\alpha]_D = -11°$ (c = 0.7, $CHCl_3$); ^1H NMR (500 MHz) δ 0.77 (d, 3H, *J*= 7), 0.84-0.92 (m, 10H), 0.94-1.04 (m, 2H), 1.24-1.42 (m, 6H), 1.63-1.68 (m, 2H), 2.00-2.13 (m, 4H), 3.46 (dt, 1H, *J*= 4, 10), 5.16 (m, 1H), 5.83 (m, 1 H), 5.83 (m, 1 H), 6.44 (m, 1H). NMR simulation using *NUTS (NMR Utility Transform Software, Acorn NMR) demonstrated the multiplicity of the olefin signals to originate from higher-order coupling*; ^{13}C NMR (125 MHz) δ 14.0, 16.4, 20.8, 22.1, 22.4, 23.5, 25.8, 27.4, 31.6, 32.0, 34.3, 41.4, 47.8, 81.6, 104.0, 124.4, 126.7, 149.9; FT-IR 907, 1143, 1173, 1181, 1610, 1653, 2871, 2921, 2954 cm^{-1}; HRMS calcd for $C_{18}H_{32}O$ (M^+) 264.2453, found 264.2451.

Ethyl 3-[2-isopropyl-5-methylcyclohexyloxy (1*R*, 2*S*, 5*R*)]-2*E*-propenoate (6a): To a solution of *L*-menthol (11.92 g, 76.30 mmol) in Et_2O (127 mL) was added Et_3N (10.6 mL, 76.3 mmol) and ethyl propiolate (7.30 mL, 72.5 mmol). The reaction mixture was stirred for 15 h protected from light. Evaporation and flash chromatography (5% EA/hex) provided alkoxyenoate **6a** (10.0 g, 54%): R_f 0.52 (20% EA/hex); $[\alpha]_D = -65°$ (c = 0.8, $CHCl_3$); ^1H NMR (360 MHz) δ 0.75 (d, 3H, *J*= 7), 0.88 (d, 3H, *J*= 7), 0.91 (d, 3H, *J*= 7), 0.89-1.08 (m, 3H), 1.26 (t, 3H, *J*= 7), 1.35-1.45 (m, 2H), 1.64-1.70 (m, 2H), 1.96-2.06 (m, 2H), 3.70 (dt, 1H, *J*= 4,11), 4.14 (q, 2H, *J*= 7), 5.23 (d, 1H, *J*= 12.5), 7.53 (d, 1H, *J*= 12.5); ^{13}C NMR (125 MHz) δ 14.3, 16.2, 20.4, 21.8, 23.4, 25.8, 31.3, 34.0, 40.7, 47.4, 59.4, 83.0, 96.7, 162.0, 168.1; FT-IR 1041, 1124, 1200, 1456, 1619, 1640, 1707, 2870, 2924, 2955 cm^{-1}; Anal. Cald. for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30. Found: C, 70.86; H, 10.06. HRMS calcd for $C_{15}H_{26}O_3$ $(M+Na)^+$: 277.1780; found 277.1771.

Ethyl 3-[*trans*-2-phenylcyclohexyloxy-(*RS*)]-2*E*-propenoate (6b) was prepared by a similar procedure from (*RS*)-*trans*-2-phenylcyclohexanol (5.35 g, 30.4 mmol) in 92% yield (7.65 g) after flash chromatography (4% EA/hex, Et_3N pretreated silica): R_f 0.13 (10% EA/hex); ^1H NMR (300 MHz) δ 1.20 (t, 3H, *J*= 7), 1.27-1.62 (m, 4H), 1.76-1.97 (m, 3H), 2.19-2.23 (m, 1H), 2.69 (app dt, 1H, *J*= 3.5, 12), 3.98 (dt, 1H, *J*= 4.5, 10.5), 4.07 (q, 2H, *J*= 7), 5.08 (d, 1H, *J*= 12), 7.17-7.31 (m, 6H); ^{13}C NMR (75 MHz) δ 14.2, 24.6, 25.5, 32.1, 33.5, 49.9, 59.4, 85.3, 96.5, 126.5, 127.4, 128.4, 142.5, 161.9, 168.0; FT-IR 2980, 1702, 1637, 1618, 1448, 1258, 1171, 973 cm^{-1}; HRMS calcd for $C_{17}H_{22}O_3$ $(M+H)^+$ 275.1647, found 275.1643.

3-[2-Isopropyl-5-methylcyclohexyloxy (1*R*, 2*S*, 5*R*)]-2*E*-propenol (7a). To a -78 °C solution of **6a** (3.0 g, 11 mmol) in Et_2O (78 mL) was added DIBAL (25 mL, 1.0 M in hexane). After 10 h, the rxn was allowed to warm to 0 °C. Following the addition of MeOH, the reaction mixture was filtered through Celite and evaporated to yield a quantitiative yield (2.49 g, 100%) of the allylic alcohol. Following flash chromatography (15% EA/hex, Et_3N pretreated silica), **7a** was obtained yields ranging from 60 - 73%: R_f 0.25 (20% EA/hex); $[\alpha]_D = -45°$ (c = 2.6, Et_2O); ^1H NMR (500 MHz) δ 0.73 (d, 3H, *J*= 7), 0.86 (d, 3H *J*= 7), 0.88 (d, 3H, *J*= 7), 0.78-1.02 (m, 3H), 1.27-1.38 (m, 2H), 1.54 (br s, 1H), 1.60-1.65 (m, 2H), 2.00-2.27 (m, 2H), 3.47 (dt, 1H, *J*= 4, 10.5), 3.99 (d, 2H, *J*= 7.5), 5.08 (dt, 1H, *J*= 7.5, 12.5), 6.35 (d, 1H, *J*= 12.5); ^{13}C NMR (125 MHz) δ 16.3, 20.6, 22.0, 23.3, 25.7, 31.4, 34.2, 40.8, 47.6, 60.7, 80.7, 103.7, 149.6; FT-IR 3353-3303, 2870, 1648, 1455, 1385, 1369, 1240, 1154, 1094, 1039, 925 cm^{-1}; Anal Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 74.70; H, 11.79; HRMS calcd for $C_{13}H_{24}O_2$ (M^+): 212.1776; found 212.1773.

3-[*trans*-2-phenylcyclohexyloxy (*RS*)]-2*E*-propenol (7b) was prepared from **6b** (450 mg, 1.64 mmol) by a similar procedure and was isolated as a white solid in 73% yield (280 mg) after flash chromatography (20% EA/hex, Et_3N pretreated silica): R_f 0.20 (20% EA/hex); mp 70-71 °C; ^1H NMR (300 MHz) δ 0.84 (br s, 1H), 1.26-1.95 (m, 7H), 2.17-2.23 (m, 1H), 2.64 (ddd, 1H, *J*= 3.5, 10.5, 12), 3.73-3.84 (m, 3H), 4.89 (dt, 1H, *J*= 7.5, 12), 6.00 (d, 1H, *J*= 12), 7.17-7.22 (m, 3H), 7.26-7.31 (m, 2H); ^{13}C NMR (75 MHz) δ 24.8, 25.8, 32.4, 33.7, 50.6, 60.5, 83.3, 103.6, 126.3, 127.9, 128.3, 143.6, 149.8; FT-IR 3202-3176, 2930, 2888, 2856, 1671, 1175, 1037, 1027, 992, 924, 698 cm^{-1}; HRMS calcd for $C_{15}H_{20}O_2$ $(M + Na)^+$, 255.1361 found 255.1355.

3-[2-Isopropyl-5-methylcyclohexyloxy-(1*R*, 2*S*, 5*R*)]-2*E*-propenal (8a). To a solution of **7a** (1.23 g, 5.79 mmol) in CH_2Cl_2 was added activated 4 Å powdered, molecular sieves (2.9 g, 500 mg/mmol), *N*-

methylmorpholine *N*-oxide (NMO, 1.02 g, 8.69 mmol), and tetra-*n*-propylammonium perruthenate (TPAP, 183 mg, 0.579 mmol). The reaction mixture was stirred at RT for 45 min, filtered through a plug of Et_3N pretreated silica, and washed with EtOAc. Evaporation provided aldehyde **8a** (1.21 g, 100%) as a colorless oil: R_f 0.3 (20% EA/hex); $[\alpha]_D = -87°$ (c = 1.8, Et_2O); ^1H NMR (500 MHz) δ 0.76 (d, 3H, *J*= 7), 0.90 (d, 3H, *J*= 7), 0.93 (d, 3H, *J*= 7), 0.87-1.13 (m, 3H), 1.42-1.48 (m, 2H), 1.69-1.72 (m, 2H), 1.98-2.05 (m, 2H), 3.82 (dt, 1H, *J*= 4, 11), 5.63 (dd, 1H, *J*= 8, 12), 7.30 (d, 1H, *J*= 12), 9.32 (d, 1H, *J*= 8); ^{13}C NMR (125 MHz) δ 16.3, 20.5, 21.9, 23.4, 26.0, 31.4, 34.0, 40.6, 47.4, 84.3, 110.8, 170.3, 191.2; FT-IR 1138, 1214, 1250, 1455, 1611, 1634, 1672, 2871, 2926, 2956 cm^{-1}; HRMS calcd for $C_{13}H_{22}O_2$ $(M+H)^+$: 211.1698; found 211.1701.

3-[*trans*-2-phenylcyclohexyloxy (*RS*)]-2*E*-propenal (8b) was prepared similarly from alcohol **7b** (270 mg, 1.16 mmol) in 93% yield (248 mg) as a white solid: R_f 0.30 (20% EA/hex); mp 67-69 °C; ^1H NMR (500 MHz) δ 1.32-1.48 (m, 2H), 1.51-1.64 (m, 2H), 1.79-1.82 (m, 1H), 1.91-1.99 (m, 2H), 2.19-2.23 (m, 1H), 2.73 (ddd, 1H, *J*= 4, 10, 12.5), 4.03 (dt, 1H, *J*= 4.5, 10.5), 5.43 (dd, 1H, *J*= 8, 12.5), 6.83 (d, 1H, *J*= 12.5), 7.16-7.22 (m, 3H), 7.28 (t, 2H, *J*= 7.5), 9.02 (d, 1H, *J*= 8); ^{13}C NMR (125 MHz) δ 24.6, 25.4, 32.1, 33.1, 50.2, 87.1, 110.4, 127.0, 127.6, 128.6, 142.0, 170.4, 191.2; FT-IR 2937, 2859, 1666, 1631, 1611, 1260, 1119, 999, 943, 757, 2937 cm^{-1}; HRMS calcd for $C_{15}H_{18}O_2$ $(M+H)^+$ 231.1385, found 231.1394.

1*E*,3-Butadiene, [2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether (9a). To a -78 °C suspension of methyl triphenylphosphonium bromide (420 mg, 1.17 mmol) in THF (5.9 mL) was added *n*-BuLi (0.20 mL, 2.4 M in hexanes). The reaction was warmed to RT and stirred until complete dissolution was observed, then recooled to -78 °C whereupon a solution of aldehyde **8a** (247 mg, 1.17 mmol) in THF (1 mL) was added via cannula. The reaction was brought to RT and, after 30 min, quenched by the addition of H_2O and hexane. The aqueous layer was extracted with hexane. The combined organic layers were dried over magnesium sulfate, concentrated, and purified by flash chromatography (100% hexane, Et_3N pretreated silica) to afford dienol ether **9a** (156 mg, 64%): R_f 0.95 (20% EA/hex); $[\alpha]_D = -40°$ (c = 2.5, Et_2O); ^1H NMR (300 MHz) δ 0.77 (d, 3H, *J*= 7), 0.89 (d, 3H, *J*= 7), 0.91 (d, 3H, *J*= 7), 0.83-1.06 (m, 3H), 1.25-1.42 (m, 2H), 1.62-1.67 (m, 2H), 1.97-2.13 (m, 2H), 3.50 (dt, 1H, *J*= 4, 11), 4.77 (d, 1H, *J*= 10), 4.94 (d, 1H, *J*= 17), 5.62 (app t, 1H, *J*= 11.5), 6.19 (app dt, 1H, *J*= 17, 10.5), 6.48 (d, 1H, *J*= 12); ^{13}C NMR (75 MHz) δ 16.3, 20.7, 22.0, 23.4, 25.8, 31.4, 24.2, 41.1, 47.6, 81.2, 108.2, 110.8, 133.6, 150.5; FT-IR 991, 1144, 1155, 1184, 1637, 1653, 2870, 2924, 2956 cm^{-1}; HRMS calcd for $C_{14}H_{24}O$ (M^+): 208.1827; found: 208.1820.

1*E*,3-Butadiene, [*trans*-2-phenylcyclohexyl (*RS*)]ether (9b) was prepared from aldehyde **8b** (248 mg, 1.08 mmol) by a similar procedure in 43% yield (107 mg) after flash chromatography (3% EA/hex, Et_3N pretreated silica): R_f 0.93 (20% EA/hex); ^1H NMR (500 MHz) δ 1.32-1.57 (m, 4H), 1.76-1.79 (m, 1H), 1.86-1.97 (m, 2H), 2.20-2.24 (m, 1H), 2.67 (ddd, 1H, *J*= 4, 10.5, 12.5), 3.83 (dt, 1H, *J*= 4.5, 10), 4.70 (dd, 1H, *J*= 2, 10.5), 4.87 (dd, 1H, *J*= 2, 17), 5.46 (app t, 1H, *J*= 11.7), 6.04 (app dt, 1H, *J*= 10.5, 17), 6.20 (d, 1H, *J*= 12.5), 7.29 (t, 2H, *J*= 7.5), 7.18-7.23 (m, 3H); ^{13}C NMR (125 MHz) δ 24.8, 25.8, 32.4, 33.9, 50.2, 83.2, 108.1, 110.7, 126.3, 127.5, 128.3, 133.5, 143.4, 150.3; FT-IR 2931, 2856, 1651, 1637, 1119, 1034, 1025, 993, 800, 754 cm^{-1}; HRMS calcd for $C_{16}H_{20}O$ (M^+) 228.1514, found 228.1516.

5-Ethyl 3-[2-isopropyl-5-methylcyclohexyloxy-(1*R*, 2*S*, 5*R*)] -2*E*,4*E*-pentadienoate (10a). To a -78 °C solution of triethyl phosphonoacetate (1.27 mL, 6.38 mmol) in THF (1 mL) was added NaHMDS (7.54 mL, 1 M in THF), and, after 10 min, a solution of aldehyde **8a** (1.22 g, 5.80 mmol) in THF (1 mL). The reaction was allowed to warm to rt over 3 h. Water and Et_2O were added, and the aqueous layer was extracted with Et_2O. The combined organic layers were dried over sodium sulfate, concentrated, and purified by flash chromatography (8% EA/hex, Et_3N pretreated silica) to afford alkoxydienoate **10a** (810 mg, 50%): R_f 0.62 (20% EA/hex); $[\alpha]_D$ = -59° (c = 1.0, $CHCl_3$); ^1H NMR (500 MHz) δ 0.75 (d, 3H, *J*= 7), 0.81-0.87 (m, 1H), 0.88 (d, 3H, *J*= 7), 0.92 (d, 3H, *J*= 7), 0.96-1.06 (m, 2H), 1.26 (t, 3H, *J*= 7,), 1.30-1.43 (m, 2H), 1.63-1.68 (m, 2H), 1.98-2.05 (m, 2H), 3.62 (dt, 1H, *J*= 4.5, 11), 4.16 (q, 2H), 5.65 (d, 1H, *J*= 15), 5.70 (app t, 1H, *J*= 12 , 1), 6.79 (d, 1H, *J*= 12), 7.23 (dd, 1H, *J*= 12, 15); ^{13}C NMR (125 MHz) δ 14.4, 16.3, 20.6, 22.0, 23.4, 25.9, 31.5, 34.1, 41.2, 47.6, 59.8, 82.9, 105.9, 114.8, 143.3, 157.5, 167.7; FT-IR 2921, 2871, 1708, 1615, 1454, 1322, 1282, 1081, 1068, 1009, 919, 862 cm^{-1}; HRMS calcd for $C_{17}H_{28}O_3$ (M^+) 280.2038, found 280.2042.

5-[2-Isopropyl-5-methylcyclohexyloxy-(1*R*, 2*S*, 5*R*)]-2*E*,4*E*-pentadienol (11a) was prepared from from ester **10a** (630 mg, 2.25 mmol) in 99% yield (531 mg, without chromatography) by a similar procedure as described for **7a:** R_f 0.30 (20 % EA/hex); $[\alpha]_D$ = –49° (c = 3.0, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.75 (d, 3H, *J*= 7), 0.78-1.03 (m, 3H), 0.88 (d, 3H, *J*= 7), 0.91 (d, 3H, *J*= 7), 1.24-1.42 (m, 3H), 1.57-1.67 (m, 2H), 1.97-2.09 (m, 2H), 3.49 (dt, 1H, *J*= 4, 11), 4.10 (d, 2H, *J*= 6), 5.57 (dt, 1H, *J*= 6, 15), 5.60 (dd, 1H, *J*= 11, 12), 6.10 (dd, 1H, *J*= 11, 15), 6.46 (d, 1H, *J*= 12); (75 MHz) δ 16.3, 20.7, 22.1, 23.4, 25.8, 31.5, 34.2, 41.1, 47.7, 64.0, 81.5, 106.5, 128.5, 129.3, 150.7; FT-IR 3260-3420, 2920, 2869, 1657, 1171, 1139, 1008, 988, 969 cm^{-1}; HRMS calcd for $C_{15}H_{26}O_2$ $(M+Na)^+$ 261.1831, found 261.1831.

1-[5-Methoxy-1*E*,3*E*-pentadiene], [2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether (12a). To a 0 °C solution of alcohol **11a** (357 mg, 1.50 mmol) in DMF (7.5 mL) was added NaHMDS (1.9 mL, 1.0 M in THF) and then methyl iodide (0.10 mL, 1.7 mmol). The reaction was stirred for 1 hr at 0 °C and then quenched by the addition of H_2O (15 mL) and EtOAc (200 mL). The aqueous layer was extracted with Et_2O (3 x 150 mL). The combined organic layers were dried over magnesium sulfate, concentrated, and purified by flash chromatography (10% EA/hex, Et_3N pretreated silica) to afford alkoxydienol **12a** (145 mg, 38%): R_f 0.71 (20% EA/hex); ^{1}H NMR (500 MHz) δ 0.72 (d, 3H, *J*=7), 0.85 (d, 3H, *J*= 7), 0.87 (d, 3H, *J*= 7), 0.75-1.00 (m, 3H), 1.26-1.37 (m, 2H), 1.59-1.64 (m, 2H), 1.97-2.05 (m, 2H), 3.25 (s, 3H), 3.45 (dt, *J*= 4, 10.5 , 1H), 3.85 (d, 2H, *J*= 6.5), 5.46 (dt, 1H, *J*= 6.5, 15), 5.57 (app t, 1H, *J*= 11.5), 6.06 (dd, 1H, *J*= 11, 15), 6.41 (d, 1H, *J*= 12); ^{13}C NMR (125 MHz) δ 16.3, 20.5, 21.9, 23.5, 25.8, 31.4, 34.2, 41.1, 47.6, 57.3, 73.2, 81.2, 106.7, 122.7, 130.2, 150.4; FT-IR 2830, 2820, 1627, 1617, 1348, 1322, 1291, 1270, 1221, 844 cm^{-1}; HRMS calcd for $C_{16}H_{28}O_2$ (M^+) 252.2089, found 252.2078.

3-[2-Isopropyl-5-methylcyclohexyloxy-(1*R*, 2*S*, 5*R*)]-2-methyl-2*E*-propenal (13a). A mixture of menthol (200 mg, 1.28 mmol), 3-ethoxymethacrolein (146 mg, 1.28 mmol), and toluenesulfonic acid monohydrate (2.0 mg, 13 mmol) was stirred under vacuum (23 mm) for 24 h. Potassium carbonate was added and the mixture was stirred for 30 min before addition of Et_2O. Removal of solvent *in vacuo* provided aldehyde **13a** (288 mg, 100%): R_f 0.53 (20% EA/hex); ^{1}H NMR (500 MHz) δ 0.79 (d, 3H, *J*= 7), 0.86-0.93 (m, 1H), 0.92 (d, 3H *J*= 7), 0.94 (d, 3H, *J*= 6), 1.04 (dq, 1H, *J*= 3.5, 12), 1.17 (dt, 1H, *J*= 11, 12), 1.48 (m, 2H), 1.67 (s, 3H), 1.67-1.73 (m, 2H), 1.98-2.02 (m, 2H), 3.77 (dt, 1H, *J*= 4, 11), 7.03 (s, 1H), 9.20 (s, 1H); (125 MHz) δ 6.5, 16.5, 20.5, 21.9, 23.7, 26.2, 31.6, 34.0, 41.8, 47.6, 86.1, 119.7, 167.5, 191.8; FT-IR 981, 1213, 1247, 1454, 1637, 1670, 2725, 2871, 2924, 2958 cm^{-1}; HRMS calcd for $C_{14}H_{24}O_2$ $(M+Na)^+$ 247.1674, found 247.1665.

3-(α-Methylbenzyloxy)-2-methyl-2*E*-propenal (13c) was prepared by a similar procedure from (*R,S*)-α-methyl benzyl alcohol (307 mg, 1.97 mmol) in 88% yield (584 mg): R_f 0.29 (25% EA/hex); ^{1}H NMR (500 MHz) δ 1.66 (d, 3H, *J*= 6.5), 1.73 (s, 3H), 5.10 (q, 1H, *J*= 6.5), 6.94 (s, 1H), 7.27-7.42 (m, 5H), 9.13 (s, 1H); ^{13}C NMR (125 MHz) δ , 6.4, 23.3, 82.8, 120.4, 125.8, 128.4, 128.8, 141.1, 166.3, 191.7; FT-IR 2981, 1638, 1201, 1064, 993, 842, 698, 548 cm^{-1}; HRMS calcd for $C_{12}H_{14}O_2$ (M^+) 190.0994, found 190.0990.

2-Methyl-1*E*,3-butadiene, [2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether (14a) was prepared from **13a** in 65% yield using a similar procedure as described for **9a**: R_f 0.95 (20% EA/hex); ^{1}H NMR (500 MHz) δ 0.77 (d, 3H, *J*= 7), 0.82-1.05 (m, 3H), 0.89 (d, 3H, *J*= 7), 0.91 (d, 3H, *J*= 7), 1.8 (ddt, 2H, *J*= 12.5, 10.5, 3), 1.62-1.68 (m, 2H), 1.70 (br s, 3H), 1.97-2.01 (m, 1H), 2.10 (dsep, 1H, *J*= 3, 7), 3.42 (dt, 1H, *J*= 4, 10.5), 4.76 (d, 1H, *J*= 10.5), 4.94 (d, 1H, *J*= 17), 6.26 (s, 1H), 6.27 (dd, 1H, *J*= 10.5, 17); ^{13}C NMR (125 MHz) δ 9.0, 16.5, 20.7, 22.1, 23.7, 26.0, 31.6, 34.3, 41.8, 47.8, 82.3, 107.0, 114.1, 137.1, 147.5; FT-IR 873, 988, 1145, 1178, 1373, 1453, 1647, 2870, 2923, 2955 cm^{-1}; HRMS calcd for $C_{15}H_{26}O$ (M^+) 222.1984, found 222.1981.

2-Methyl-1*E*,3-butadiene, α-methylbenzyl ether (14c) was prepared in 35% yield (89 mg) from aldehyde **13c** (584 mg, 3.07 mmol) by a similar procedure as described above except that purification was conducted by bulb-to-bulb distillation: R_f 0.80 (20% EA/hex); ^{1}H NMR (500 MHz) δ 1.55 (d, 3H, *J*= 7), 1.79 (d, 3H, *J*= 1), 4.79 (d, 1H, *J*= 11), 4.82 (q, 1H, *J*= 7), 4.96 (d, 1H, *J*= 17), 6.18 (dd, 1H, *J*= 11, 17), 6.19 (s,

1H,), 7.27-7.37 (m, 5H); ^{13}C NMR (125 MHz) δ 9.0, 23.7, 80.0, 107.9, 115.3, 125.9, 127.7, 128.5, 128.7, 136.9, 146.7; FT-IR 3087, 2979, 2929, 1649, 1450, 1169, 1119, 1071, 761, 700 cm^{-1}.

3-[2-Isopropyl-5-methylcyclohexyloxy-(1*R*, 2*S*, 5*R*)]-3*E*-buten-2-one (15a) was prepared in 95% yield (420 mg) from menthol (307 mg, 1.97 mmol) and *trans*-4-methoxy-3-buten-2-one (0.20 mL, 2.0 mmol) by a similar procedure as desribed for **13a**. Spectral characteristics were identical to literature reports. [39]

(1*E*)3-Methyl-1,3-butadiene, [2-isopropyl-5-methylcyclohexyl ether-(1*R*, 2*S*, 5*R*)] (16a) was prepared in 43% yield (89 mg) from ketone **15a** (208 mg, 0.927 mmol) by a similar procedure as described for **9a**: R_f 0.95 (20% EA/hex); $[\alpha]_D = -22°$ (c = 2.5, $CHCl_3$); ^{1}H NMR (500 MHz) δ 0.77 (d, 3H, *J*= 7), 0.89 (d, 3H, *J*= 7), 0.92 (d, 3H, *J*= 6.5), 0.82-1.04 (m, 4H), 1.35 (ddt, 1H, *J*= 12, 10.5, 3), 1.37-1.43 (m, 1H), 1.62-1.69 (m, 2H), 2.02-2.06 (m, 1H), 2.10 (app dp, 1H, *J*= 2.5, 7), 3.50 (dt, 1H, *J*= 4, 10.5), 4.64 (s, 1H), 4.72 (s, 1H), 5.73 (d, 1H, *J*= 12.5), 6.41 (d, 1H, *J*= 12.5); ^{13}C NMR (125 MHz) δ 16.4, 19.0, 20.7, 22.1, 23.5, 25.8, 31.5, 34.3, 41.3, 47.8, 81.3, 110.3, 110.9, 139.9, 147.6; FT-IR 864, 919, 1041, 1143, 1175, 1453, 1636, 1646, 2870, 2922, 2954 cm^{-1}; HRMS calcd for (M^+) 222.1984, found 222.1978.

Photooxygenations-General Conditions: A 0.1M solution of the dienol ether in 0.02 mM TPP / CH_2Cl_2 was cooled to 0 °C in a jacketed photolysis cell. Under continuous sparging with oxygen, the solution was irradiated with a 200 W incandescent microscope illuminator from a distance of 10-15 cm until the reaction was complete according to TLC or NMR. Reactions were concentrated *in vacuo* and then redissolved in $CDCl_3$. (Hydroperoxides were stabilized with a few drops of 0.1% solution of BHT in CH_2Cl_2 prior to concentration.) Diastereomeric ratios were determined from resolved signals in the crude ^{1}H NMR spectrum. Following NMR, the reconcentrated samples were directly subjected to chromatography on silica gel.

6-Butyl-3-[2-Isopropyl-5-methylcyclohexoxy-(1*R*, 2*S*, 5*R*)]-3,6-dihydro-1,2-dioxine (17a) was obtained from alkoxy diene (1Z,3E) **5a** (225 mg, 0.85 mmol) in 63% yield (159 mg) as a 1.56 : 1 mixture of diastereomers which could be separated by HPLC (1% EA/hex): R_f 0.65 (10% EA/hex)

Major isomer: $[\alpha]_D = -11°$ (c = 0.1, $CDCl_3$); ^{1}H NMR (300 MHz) δ 0.76 (d, 3H, *J* = 7); 0.81-1.83 (m, 22H), 2.12 (apparent dp, 1H, *J* = 2, 7), 2.24-2.31 (m, 1H), 3.39 (dt, 1H, *J* = 4,), 4.26 (m, 1H), 5.05 (d, 1H, *J* = 3), 5.87 (ddd, 1H, *J* = 1, 4, 10), 6.12 (ddd, 1H, *J* = 1, 4, 10); ^{13}C NMR (75 MHz) δ 14.6, 17.0, 21.7, 22.8, 23.2, 24.0, 26.3, 28.7, 32.47, 32.51, 35.0, 44.0, 49.1, 78.9, 81.7, 99.2, 123.0, 132.2; FT-IR 3053, 2947, 2920, 2870, 1456, 1385, 1344, 1099, 1051, 1014, 991 cm^{-1}; Anal. Calcd for $C_{18}H_{32}O_3$: C, 72.93; H, 10.88. Found: C, 73.10; H, 10.95. *Minor isomer:* ^{1}H NMR (360 MHz) δ 0.85 (d, 3H, *J*= 7 , 3H), 0.88-1.08 (m, 11H), 1.24-1.68 (m, 10H), 1.76-1.86 (m, 1H), 1.99-2.05 (m, 1H), 2.35 (app dp, 1H, *J*= 2, 7), 3.57 (dt, 1H, *J*= 4.5, 11), 4.23 (m, 1H), 5.13 (d, 1H, *J*= 4), 5.80 (ddd, 1H, *J*= 2, 4, 10), 6.14 (ddd, 1H, *J*= 1, 4, 10); Anal. Calcd for $C_{18}H_{32}O_3$: C, 72.93; H, 10.88. Found: C, 72.75; H, 10.65.

6-Butyl-3,6-dihydro-3-[*trans*-2-phenylcyclohexoxy-(*RS*)]-1,2-dioxine (17b) was obtained from oxygenation of (1Z,3E) **5b** (131 mg, 0.460 mmol) in 71% yield (103 mg) as a 2.9 : 1 mixture of diastereomers. The minor isomer decomposed upon chromatography (100% hexane). *Major isomer:* R_f 0.12 (5% EA/hex); ^{1}H NMR (500 MHz) δ 0.86 (t, 3H, *J*= 7), 1.24-1.70 (m, 10H), 1.73-1.77 (m, 1H), 1.83-1.90 (m, 2H), 2.27-2.30 (m, 1H), 2.57 (ddd, 1H, *J*= 3.5, 10.5, 13), 3.60 (dt, 1H, *J*= 4.5, 10.5), 4.15 (m, 1H), 4.20 (d, 1H, *J*= 3.5), 5.25 (ddd, 1H, *J*= 1.5, 3.5, 10), 5.93 (ddd, 1H, *J*= 1, 4, 10), 7.18-7.21 (m, 1H), 7.23-7.30 (m, 4H); ^{13}C NMR (125 MHz) δ 13.9, 22.5, 25.3, 25.8, 28.0, 31.7, 32.6, 34.7, 51.4, 78.2, 83.2, 97.8, 122.1, 126.4, 128.0, 128.2, 131.1, 144.1; FT-IR 2928, 2857, 1467, 1463, 1393, 1379, 1326, 1009, 973, 738 cm^{-1}; HRMS (FAB, 3-NBA + Li) calcd for $C_{20}H_{28}O_3$ $(M + Li)^+$ 323.2198, found 323.2204.

3-[2-Isopropyl-5-methylcyclohexoxy-(1*R*, 2*S*, 5*R*)]-3,6-dihydro-1,2-dioxine (18a) was obtained from alkoxy diene **9a** (50 mg, 0.24 mmol) in 86% yield (50 mg) as a 1.3 : 1 mixture of diastereomers separable by flash chromatography (5% EA/hex): FT-IR (neat) 2870, 2855, 2849, 1737, 1727, 1712, 1329, 1239, 941, 921, 801 cm^{-1}; HRMS calcd for $C_{14}H_{24}O_3$ $(M+Li)^+$ 247.1885, found 247.1876

Major Isomer: R_f 0.21 (5% EA/hexane); $[\alpha]_D = -28°$ (c = 0.3, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.86 (d, 3H, *J*= 7), 0.91 (d, 3H, *J*= 7), 0.93 (d, 3H, *J*= 7), 0.77-1.06 (m, 3H), 1.26-1.35 (m, 2H), 1.63-1.71 (m, 2H), 2.00-2.07 (m, 1H), 2.38 (app dp, 1H, *J*= 2, 7), 3.58 (dt, 1H, *J*= 4, 10.5), 4.32 (dd, 1H, *J*= 4.5, 17), 4.78 (d, 1H,

J= 17), 5.19 (br s, 1H), 5.89 (d, 1H, *J*= 10), 6.19 (dd, 1H, *J*= 4.5, 10); ^{13}C NMR (75 MHz) δ 15.5, 21.0, 22.2, 23.0, 25.0, 31.5, 34.4, 40.5, 47.8, 69.0, 77.2, 94.4, 123.4, 128.3

Minor Isomer: R_f 0.28 (5% EA/hexane); $[\alpha]_D$ = +15° (c = 0.1, $CHCl_3$); ^{1}H NMR (300 MHz) δ 0.77 (d, 3H, *J*= 7), 0.90 (d, 3H, *J*= 7), 0.91 (d, 3H, *J*= 7), 0.80-1.03 (m, 2H), 1.09-1.41 (m, 3H), 1.58-1.66 (m, 2H), 2.13 (app dp, 1H, *J*= 2, 7), 2.27 (m, 1H), 3.41 (dt, 1H, *J*= 4.5, 10.5), 4.34 (dd, 1H, *J*= 4.5, 17), 4.76 (d, 1H, *J*= 17), 5.11 (br s, 1H), 5.94 (d, 1H, *J*= 10), 6.17 (dd, 1H, *J*= 4.5, 10); ^{13}C NMR (75 MHz) δ 16.3, 21.0, 22.2, 23.3, 25.0, 31.8, 34.3, 43.2, 48.4, 69.1, 81.0, 98.9, 123.0, 128.0

3,6-Dihydro-3-[*trans*-2-phenylcyclohexoxy-(*RS*)]-1,2-dioxine (18b). Oxygenation of **9b** (100 mg, 0.438 mmol) by a similar procedure furnished a 2.0 : 1 mixture of diastereomeric endoperoxides **18b** in 79% yield (90 mg) following flash chromatography (4% EA/hex): R_f 0.32 (10% EA/hexane); HRMS calcd for $C_{16}H_{20}O_3$ $(M+Na)^+$ 283.1310, found 283.1306. *Major Isomer:* ^{1}H NMR (360 MHz) δ 1.25-1.94 (m, 7H), 2.22-2.30 (m, 1H), 2.58 (dt, 1H, *J*= 3, 11), 3.62 (dt, 1H, *J*= 4, 10.5), 4.22 (dd, 1H, *J*= 4.5, 17), 4.26 (br s, 1H), 4.62 (d, 1H, *J*= 17), 5.31 (d, 1H, *J*= 10), 5.96 (dd, 1H, *J*= 4.5, 10). *Minor Isomer:* ^{1}H NMR (360 MHz) δ 1.25-1.94 (m, 7H), 2.22-2.30 (m, 1H), 2.64 (dt, 1H, *J*= 3, 11), 3.98 (dt, 1H, *J*= 4, 10.5), 4.07 (dd, 1H, *J*= 4.5, 17), 4.57 (d, 1H, *J*= 17), 5.14 (br s, 1H), 5.52 (d, 1H, *J*= 10), 5.96 (dd, 1H, *J*= 4.5, 10 , 1H).

3-[2-Isopropyl-5-methylcyclohexoxy-(1*R*, 2*S*, 5*R*)]-6-methoxymethyl-3,6-dihydro-1,2-dioxine (19a). Photooxygenation of dienol ether **12a** (57 mg, 0.226 mmol) furnished, after flash chromatography (10% EA/hex), an inseparable 1.25 : 1 diastereomeric mixture of endoperoxides **19a** (25 mg, 35% yield) accomanied by alkoxyenal **8a** (9 mg, 19%): R_f 0.35 (20% EA/hex); ^{1}H NMR (500 MHz) δ 0.76 and 0.84 (each d, total 3H, *J*= 7) 0.85-1.16 (m, 9H, both isomers), 1.24-1.41 (m, 2H, both isomers), 1.58-1.70 (m, 2H, both isomers), 1.98-2.04 (m, 0.5H), 2.12 and 2.34 (app dp, total 1H, each *J*= 3, 7), 2.27-2.31 (m, 0.5H), 3.33-3.56 (m, 2H), 3.369 and 3.372 (each s, total 3H), 3.46 and 3.58 (each dt, total 1H, *J*= 4, 11), 4.85-4.89 (m, 1H, both isomers), 5.12-5.13 and 5.19-5.20 (each m, total 1H), 5.91 and 5.97 (each ddd, total 1H, *J* = 2,4,10 and 2,3,10), 6.03 and 6.04 (each app dt, total 1H, *J*= 1, 10); ^{13}C NMR (125 MHz) δ both isomers 15.7, 16.3, 20.9, 21.0, 22.15, 22.24, 23.2, 23.3, 25.2, 25.7, 31.5, 31.8, 34.3, 34.4, 40.9, 43.2, 47.8, 48.4, 71.98, 72.01, 76.5, 77.2, 77.4, 77.6, 81.2, 93.9, 98.8, 124.7, 125.0, 128.8, 128.9; FT-IR 2953, 2924, 2869, 1715, 1454, 1197, 1129, 1087, 991, 742 cm^{-1}; HRMS calcd for $C_{16}H_{28}O_4Na$ $(M+Na)^+$ 307.1885, found 307.1880.

1-[1-Hydroperoxy-2-methylene-3-butene], 2-isopropyl-5-methylcyclohexyloxy-(1*R*, 2*S*, 5*R*)] (20a). Photooxygenation of dienol ether **14a** (100 mg, 0.450 mmol), performed to low conversion due to the tendency of the initial diene hydroperoxide product to undergo a second cycloaddition, furnished a 2.3 : 1 diastereomeric mixture of hydroperoxides **20a**: R_f 0.56 (20% EA/hex): *Major isomer:* ^{1}H NMR (360 MHz) δ 0.70 (d, 3H, *J*= 7), 0.75-1.16 (m, 3H), 0.88 (d, 3H, *J*= 7), 0.93 (d, 3H, *J*= 7), 1.28-1.43 (m, 3H), 1.62-1.69 (m, 2H), 2.12 (app dp, 1H, *J*= 3, 7), 2.24-2.30 (m, 1H), 3.38 (dt, 1H, *J*= 4, 11), 5.15 (d, 1H, *J*= 11), 5.36 (s, 1H), 5.46 (s, 1H), 5.49 (s, 1H), 5.52 (d, 1H, *J*= 18), 6.33 (dd, 1H, *J*= 11, 18), 7.94 (s, 1H, OO**H**).

Minor isomer: ^{1}H NMR (360 MHz) δ 0.71-1.07 (m, 3H), 0.85 (d, 3H, *J*= 7), 0.89 (d, 3H, *J*= 7), 0.94 (d, 3H, *J*= 7), 1.31-1.41 (m, 2H), 1.61-1.69 (m, 2H), 1.93-1.98 (m, 1H), 2.35 (dsep, 1H, *J*= 2.5, 7), 3.62 (dt, 1H, *J*= 4, 11), 5.16 (d, 1H, *J*= 11), 5.35 (s, 1H), 5.52 (d, 1H, *J*= 18), 5.53 (s, 1H), 5.55 (s, 1H), 6.35 (dd, 1H, *J*= 11, 18), 7.85 (s, 1H, OO**H**).

1-[1-Hydroperoxy-2-methylene-3-butene], [α-methylbenzyl (*RS*)] ether (20c): Photooxygenation of dienol ether **14c** (100 mg, 0.450 mmol) furnished **20c** as a 2.5 : 1 mixture of diastereomers: R_f 0.17 (5% EA/hex); ^{1}H NMR (360 MHz) δ 1.49 (d, 0.3x3H, *J*= 7), 1.55 (d, 0.7 x 3H, *J*= 7), 4.74 (q, 0.3H, *J*= 7), 5.03 (q, 0.7H, *J*= 7), 5.08 (d, 0.7H, *J*= 11), 5.15 (d, 0.3H, *J*= 11), 5.35-5.57 (multiple singlets, 4H, both isomers), 6.28 (dd, 0.7H, *J*= 11, 17), 6.34 (dd, 0.3H, *J*= 11, 17), 7.26-7.42 (m, 5H, both isomers).

3-[2-Isopropyl-5-methylcyclohexoxy-(1*R*, 2*S*, 5*R*)]-5-methyl-3,6-dihydro-1,2-dioxine (21a). Oxygenation of **16a** (378 mg, 1.70 mmol) furnished a 1.14 : 1 diastereomeric mixture of endoperoxides **21a** (393 mg, 90%) which were separable by flash chromatography (2% EA/hex): FT-IR 1024, 1052, 1066, 1101, 1449, 1689, 1725, 2869, 2921, 2954 cm^{-1}; HRMS calcd for $C_{15}H_{26}O_3Li$ $(M+Li)^+$ 261.2042, found 261.2039.

Isomer A: R_f 0.33 (95% hexane/Et_2O); $[\alpha]_D$ = –25° (c = 0.6, $CHCl_3$); ^1H NMR (500 MHz) δ 0.75 (d, 3H, *J*= 7), 0.77-1.00 (m, 2H), 0.88 (d, 3H, *J*= 6.5), 0.89 (d, 3H, *J*= 6.5), 1.07 (dt, 1H, *J*= 11, 12), 1.29 (br t, 1H, *J*= 11), 1.35-1.42 (m, 1H), 1.58-1.63 (m, 2H), 1.72 (s, 3H), 2.12 (app dp, 1H, *J*= 2, 7), 2.23-2.27 (m, 1H), 3.38 (dt, 1H, *J*= 4, 10.5), 4.10 (d, 1H, *J*= 16), 4.62 (d, 1H, *J*= 16), 5.07 (br s, 1H), 5.63 (br s, 1H); ^{13}C NMR (125 MHz) δ 16.3, 17.9, 21.0, 22.1, 23.2, 25.6, 31.7, 34.2, 43.3, 48.4, 72.3, 80.7, 98.9, 117.3, 136.4.

Isomer B: R_f 0.27 (95% hexane/Et_2O); $[\alpha]_D$ = –28° (c = 2.0, $CHCl_3$); ^1H NMR (500 MHz) δ 0.79-1.04 (m, 3H), 0.83 (d, 3H, *J*= 7), 0.88 (d, 3H, *J*= 7), 0.90 (d, 3H, *J*= 7), 1.27 (br t, 1H, *J*= 11), 1.30-1.38 (m, 1H), 1.62-1.66 (m, 2H), 1.73 (s, 3H), 1.99 (br d, 1H, *J*= 12), 2.36 (app dp, 1H, *J*= 2, 7), 3.52 (dt, 1H, *J*= 4, 10.5), 4.10 (d, 1H, *J*= 16.5), 4.60 (d, 1H, *J*= 16.5), 5.13 (br s, 1H,), 5.56 (br s, 1H); ^{13}C NMR (125 MHz) δ 15.3, 18.1, 21.0, 22.2, 22.9, 24.9, 31.5, 34.3, 40.6, 47.7, 72.2, 76.5, 94.5, 117.6, 136.6.

PTAD cycloadduct of 1*Z*,3*E*-octadiene, 2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether (22): To a 0 °C solution of dienol ether (1Z,3E)-**5a** (8.3 mg, 0.031 mmol) in d_8-THF (0.5 mL) in an NMR tube was added 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD, 5.6 mg, 0.032 mmol) in d_8-THF (0.5 mL). Complete conversion to a 1.2 : 1 mixture of diastereomrs **22** was observed after 3 min: ^1H NMR (300 MHz, d_8-THF) δ 0.59-2.17 (m, 25H), 3.67 (dt, 0.45H, *J* = 4, 10.5), 3.81 (dt, 0.55H*J* = 4, 10.5 , 1.2 H), 5.65 (d, *J* = 4 , 1.0 H), 5.79 (d, *J* = 4), 1.2 H), 5.85-5.91 (m, 1.2 H), 6.04-6.16 (m, 2.8 H), 7.27-7.59 (5H).

1*Z*,3*E*-nonadiene, 2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether (23):
To a RT solution of tetrakis(triphenylphosphine) palladium (500 mg, 0.558 mmol) in isopropylamine was added (*E*)-1-iodoheptene (1.92 g, 8.56 mmol). The mixture was stirred for 30 min whereupon alkynyl ether **1a** (2.01 g, 11.2 mmol) and a solution of copper (I) iodide (163 mg, 1.12 mmol) in isopropylamine (5 mL) were sequentially added. The resulting orange solution was stirred in the dark for 6 h and then diluted with hexane. The solution was washed with sat. aq. ammonium chloride and the aqueous layer was back extracted with hexane. The combined organic layers were dried over sodium sulfate and concentrated. After flash chromatography (100% hexane, Et_3N pretreated silica) was isolated 3*E*-nonen-1-ynyl,[2-isopropyl-5-methylcyclohexyl (1*R*, 2*S*, 5*R*)] ether as a clear, light yellow oil (2.06 g, 87%): R_f 0.34 (100% hexane); $[\alpha]_D$=-53° (c = 1.4); ^1H NMR (300 MHz) 0.83 (d, 3H, *J*=6.9), 0,86-1.56 (20H), 1.64-1.71 (m, 2H) 2.02-2.10 (m, 2H), 2.15 (apparent dp, 1H, *J*=2.9, 6.9), 2.24-2.30 (m, 1H), 3.83 (dt, 1H, *J*=4.5, 11.0), 5.44 (dt, 1H, *J*=15.5, 1.7), 5.92 (dt, 1H, *J*=15.7, 6.9); ^{13}C NMR (75 MHz) 14.0, 16.3, 20.6, 22.0, 22.5, 23.4, 25.9, 28.8, 31.4, 31.6, 32.9, 34.0, 39.2, 39.8, 46.9, 88.2, 96.2, 109.3, 140.8; FT-IR 2247, 1717 cm-1.

A septum-sealed flask containing a solution of nickel(II) acetate (45 mg, 0.18 mmol) in 5 mL of absolute ethanol placed was flushed with hydrogen and then allowed to stand under a balloon of the same gas. A solution of sodium borohydride (6.9 mg, 0.18 mmol) in 3 mL of absolute ethanol was added. After an additional 20 min, ethylenediamine (0.045 mL, 0.72 mmol) was added followed by a solution of the enynol ether (53 mg, 0.19 mmol) in ethanol (2 mL) were added. After stirring for an additinal hour, 1h, hydrogen was purged and the reaction mixture was diluted with hexane. After washing with 10% aq. $NaHCO_3$, the organic layer was dried over Na_2SO_4. Concentration, followed by flash chromatography (100% hexane, Et_3N pretreated silica) afforded a clear, colorless oil (42 mg, 82%) containing an 82:18 mixture of the desired dienol ether and the over reduced enol ether. The two were separated using HPLC (100% Hexane, 21 mm x 25 cm Si column) to afford the pure dienol ether : R_f0.34 (100% hexane); $[\alpha]_D$ = -53° (c = 0.9, Hexane); ^1H NMR (500 MHz) 0.78 (d, 3H, *J*=6.9), 0.86-1.41 (20H), 1.63-1.67 (m, 2H), 1.99-2.17 (m, 4H), 3.40 (dt, 1H, *J*=4.3, 10.7), 4.99 (dd, 1H, *J*=10.7, 6.4), 5.51 (dt, 1H, *J*=15.5, 6.9), 5.92 (d, 1H, *J*=6.4), 6.36 (dd, 1H, *J*=11.0, 14.8); ^{13}C NMR (125 MHz) 143.9, 130.5, 123.3, 106.4, 82.3, 47.9, 41.7, 34.4, 32.9, 31.6, 31.5, 29.4, 26.0, 23.7, 22.6, 22.1, 20.8, 16.5, 14.1; FT-IR 1653, 1616 cm^{-1}.

6-Pentyl-3-[2-Isopropyl-5-methylcyclohexoxy-(1*R*, 2*S*, 5*R*)]-3,6-dihydro-1,2-dioxine (24a): A solution of dienol ether **23** (279 mg, 1.00 mmol) in 15 mL of a 0.001 M solution of TPP in CH_2Cl_2 was cooled to 0 °C in a jacketed pyrex cell and aspirated with oxygen. The solution was photolyzed with a 200 W visible illuminator from a distance of 12 cm for 25 min. The crude reaction mixture was concentrated and purified by

flash chromatography (0.05% EA/Hexane) to furnish 201 mg (65%) of dioxine **24a** as a 1.6 : 1 mixture of diastereomes which could be separated by HPLC (2% EA/Hex):
Major isomer: (3S,6R) Rf 0.61 (10% EA/Hex); $[\alpha]_D$=+ 1.7° (c=1.0, hex); ^{1}H NMR (300 MHz) 0.78 (d, 3H, *J*=6.9), 0.81-1.83 (24H), 2.14 (apparent dp, 1H, *J*=2.4, 7.2), 2.27-2.34 (m, 1H), 3.41 (dt, 1H, *J*=4.5, 10.8), 4.28 (m, 1H), 5.07 (d, 1H, *J*=3.3), 5.87 (ddd, 1H, *J*=1.6, 3.3, 10.3), 6.14 (ddd, 1H, *J*=1.2, 4.3, 10.3); ^{13}NMR (75 MHz) 131.6, 122.3, 98.6, 81.0, 78.3, 48.5, 43.3, 34.3, 32.1, 31.8, 31.7, 25.7, 25.6, 23.3, 22.6, 22.2, 21.1, 16.3, 14.0; Anal. Calcd for $C_{19}H_{34}O_3$: C, 73.50%; H, 11.04 %. Found: C, 73.77%; H, 11.32%.
Minor isomer: (3R,6S) Rf 0.65 (10% EA/Hex); $[\alpha]_D$=- 161° (c = 0.1, hex); ^{1}H NMR (300 MHz) 0.85 (d, 3H, *J*=6.9), 0.88-1.88 (24H), 1.99-2.08 (m, 1H), 2.36 (apparent dp, 1H, *J*=2.4, 7.2), 3.57 (dt, 1H, *J*=4.5, 10.8), 4.24 (m, 1H), 5.14 (d, 1H, *J*=3.3), 5.81 (ddd, 1H, *J*=1.6, 3.3, 10.3), 6.16 (ddd, 1H, *J*=1.2, 4.3, 10.3); ^{13}NMR (75 MHz) 131.8, 122.8, 93.8, 78.1, 76.5, 47.9, 40.5, 34.5, 32.3, 31.8, 31.6, 25.7, 25.2, 23.1, 22.6, 22.3, 21.1, 15.6, 14.1; Anal. Calcd for $C_{19}H_{34}O_3$: C, 73.50%; H, 11.04%. Found: C, 74.01%; H, 11.53%.
5(*R*)-pentyl-2(5H)-furanone (25) and **(3R,6R)-3,6-dihydro-3-methoxy-6-pentyl-1,2-dioxine (26)**: Into a solution of dioxine **24a** (31 mg, 0.1 mmol) in MeOH (2 mL) was added TsOH•H_2O (8 mg, 0.04 mmol). The solution was brought to reflux for 6 h and then quenched with water. The hexane extract was concentrated and purified with flash chromatography (10% EA/Hex) to afford the furanone **25** as a colorless oil for which the stereochemistry was assigned on the basis of comparison with reported literature data.[29] Rf=0.29 (10% EA/Hex); $[\alpha]_D$=-90°(c=0.3, hexane); ^{1}H NMR (300 MHz) 0.87 (t, 3H, *J*=6.9), 1.24-1.45 (m, 8H), 1.69 (m, 2H), 5.02 (td,1H, *J*=6.2, 1.9), 6.08 (dd, 1H, *J*=5.7, 1.9), 7.44 (dd,1H, *J*=5.7, 1.4); ^{13}C NMR (75 MHz) 173.1, 156.3, 121.5, 83.4, 33.2, 31.4, 24.6, 13.9; FT-IR 2954, 2931, 2860, 1755, 1601, 1466, 1163, 1099, 1020, 816 cm^{-1}. The furanone was accomanied by small amounts (10%) of dioxine **26**, which was assigned as 3*S*,6*S* stereochemistry on the basis of comparison with literature reports for the enantiomer.[2]

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